

**REMARKS**

Claims 2-8, 10, 12-14, 16-28, 30-33, 35, 39-42, 44 and 46-58 have been canceled. Claim 1, 15 and 29 have been amended. Support for the amended claim and added claim can be found throughout the specification and drawings of the application as filed. No new matter has been added by amending claims 2-8, 10, 12-14, 16-28, 30-33, 35, 39-42, 44 and 46-58.

1. The Examiner states, "Claims 1, 3, 6-11, 15, 29-30, 32-38 and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating senile dementia of Alzheimer's disease with the compounds wherein R1 is those defined in claim 6, A is those defined in claim 9, and B is those defined in claim 10, does not reasonably provide enablement for preventing senile dementia of Alzheimer disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Andands*, 8 USPQ 2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factor to consider when assessing if a disclosure would have required undue experimentation. The court recited eight factors:

1. the quantity of experimentation necessary,
2. the amount of direction or guidance provided,
3. the presence or absence of working examples,
4. the nature of the invention,
5. the state of the prior art,
6. the relative skill of those in the art,
7. the predictability of the art, and
8. the breadth of the claims.

The claims are broadly cover method of treating and preventing senile dementia of Alzheimer's disease with compounds defined by the general formula in claim 1, which essentially encompasses unlimited number of compounds with various structurally distinct features. The specification discloses particular compound 1 and 5 have shown excellent NGF and BDNF production/secretion

promoting activity (experimental example 1). The specification nor the prior art of record provide any guidance for one of skill in the art to use the invention in expectation of administering a therapeutically effective amount of the oxazole derivatives herein for prevention senile dementia of Alzheimer. Particularly, the exact etiology of Alzheimer's diseases has not yet been fully understood (Pillay et al). The promotion of NGF and BDNF production/secretion while has been reasonably expected to interfere the development of Alzheimer's disease, but has not been shown to be effective for preventing Alzheimer's disease. Further, the specification provide no working examples, or any rationale that compounds other than those closely related to compounds 1 and 5, i.e. the compounds wherein R1 is those defined in claim 6, A is those defined in claim 9, and B is those defined in claim 10, would be similarly effective as compounds 1 and 5, so that be useful for treating senile dementia of Alzheimer's disease. It is noted that the pharmaceutical art generally is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The court in *In re Fisher*, 427 F.2d 833, 839; 166 USPQ 18, 24 (CCPA 1970) held that, "in case involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." The more unpredictable an area, the more specific enablement is need in order to satisfy the statue. The unpredictability is more apparent where the diseases disclosed in the specification are as complex and diverse in etiology of Alzheimer's disease. Further, various structural distinct compounds herein deemed to present unpredictability as to their physiological properties. For examples, R1 herein defined as halogen or any heterocyclic groups. The difference of the sizes, shapes and electronic distribution of the R1 would certainly affect the physical and chemical properties of the compounds and thereby affects the physiological property. In the instant case, the art and the evidence presented in the instant application fails to establish support for prevention senile dementia of Alzheimer's disease, or treatment of senile dementia of Alzheimer's disease with compounds other than those closely related to compounds 1 and 5, i.e. the compounds wherein R1 is those defined in claim 6, A is those defined in claim 9, and B is those defined in claim 10, as instantly claimed. Thus it would require undue experimentation for the skilled artisan to practice the invention as broadly claimed.".

Applicants respectfully disagree. In the Office Action, the Examiner holds that the present specification fails to establish support for prevention of senile dementia of Alzheimer's disease, or treatment of senile dementia of Alzheimer's disease with compounds other than those closely related to compounds 1 and 5, i.e., the compounds wherein R1 is those defined in claim 6, A is those defined in claim 9, and B is those defined in claim 10.

Claim 1 has been amended to a "method for treating senile dementia of Alzheimer's disease".

In addition, the range of the compound of claim 1 has been limited by the definition of R<sup>1</sup> in claim 6, the definition of B in claim 10, and the definition of X in claim 12. Further, the definition of A has been amended to "a phenoxy group substituted with an alkyl group which may optionally be substituted or a C<sub>1-4</sub> alkoxy".

In the definition of A after amendment, C<sub>1-4</sub> alkoxy has been added to the definition of A in claim 9 as a substituent on the phenoxy group (support in the English specification: page 27, line 2). The compound (1) described in Experimental Example is 4-(4-chlorophenyl)-5-[3-(2-methoxyphenoxy)propyl]-2-(2-methyl-1-imidazolyl)oxazole (English specification page 29, lines 23-24), which is a compound wherein A is a phenoxy group substituted with methoxy. We believe therefore that the addition of "C<sub>1-4</sub> alkoxy" as a substituent on the phenoxy group should be admitted.

Applicants believe that the outstanding rejection is overcome by the above-mentioned amendments and request reconsideration.

2. The Examiner states, "Claims 1, 3, 6-12, 15, 29-30, 32-38 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims recited method of treating or preventing senile dementia of Alzheimer *type*. The claims, or the specification provide no clear

definition as to “Alzheimer’s type”. It is not clear what the other senile dementia is encompassed herein other than those of Alzheimer. The claims are indefinite as to the senile dementia encompassed thereby.”.

In the amended claims, the term “Alzheimer’s type” has been amended to “Alzheimer’s disease”, thus, obviating the outstanding rejection. Applicants believe that this amendment should be entered since it simply clarifies the term and request reconsideration.

3. The Examiner states, “Claims 1, 3, 6-12, 15, 29-30, 32-38 and 43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-30 of U.S. Patent No. 6,605,629 in view of Mathew et al. (WO 99/16460). Claims 21-30 in ‘629 directed to a method for promoting neurotrophin production/secretion in a mammal in need thereof by administering the compounds herein. In light of the specification, “mammal in need thereof” would apparently include senile dementia of Alzheimer’s disease (page 39, line 33 to page 40, line 22). Further, it is well-known in the art, that high neurotrophin, such as NGF, is beneficial to neurodegenerative disease, such as Alzheimer’s disease and dementia. See, e.g., pages 3 and 13 in Mathew et al. Therefore, it would have been obvious to one of ordinary skill in the art to practice the cited invention of ‘629 by treating senile dementia of Alzheimer as Alzheimer patients are those “in need thereof” and it is well established in the art that neurotrophin, such as NGF, is beneficial for patient with Alzheimer’s disease.”.

Applicants are concurrently filing herewith a Terminal Disclaimer which disclaims, with regard to pending claims of the '769 application, the terminal portion of any patent granted on this application which would extend beyond the expiration of the U.S. Patent Number 6,605,629. As such, the basis for this rejection is obviated.

The Examiner is requested to call Applicants' undersigned representative to discuss the restriction application. Applicants thank the Examiner in advance for this courtesy.

The Director is hereby authorized to charge any credits or deficiency in the fees filed (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. (46590) 66535DIV.

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Respectfully submitted,



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